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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/092,900	03/07/2002	Muralidhara Padigaru	21402-290C (CURA 590C)	1049

7590 02/24/2004

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ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/092,900	PADIGARU ET AL.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group VI (claims 13-22) drawn to isolated nucleic acid molecules, vectors comprising nucleic acid molecules, and host cells comprising vectors and subgroup ii (SEQ ID NO: 111) is acknowledged.

The restriction requirement is still deemed proper and is therefore made FINAL. Claims 1-12 and 23-26 are cancelled. Claims 13-22 as drawn to SEQ ID NO: 111 are under consideration.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Connexin-like protein and nucleic acid encoding same.

The use of the trademarks XENOMOUSE™ (p. 50), LUPRON DEPOT™ (p. 59), CREMOPHOR™ EL (p. 69), TRITON™ (p. 75), SEQCALLING™ (p. 96), GENECALLING™ (p. 483), PATHCALLING™ (p. 484), and TAQMAN™ (p. 488) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13-22 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 13-22 are directed to isolated nucleic acid molecules comprising SEQ ID NO: 111. The specification discloses a nucleic acid molecule comprising SEQ ID NO: 111 which encodes a polypeptide comprising SEQ ID NO: 112. The specification asserts that the polypeptide encoded by SEQ ID NO: 111 is a novel connexin-like polypeptide (NOV34) that bears structural similarity with mouse and human connexins (p. 204-205). The claimed polynucleotide is not supported by either a specific and substantial asserted utility or a well-established utility.

A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" use for the claimed invention. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966):

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

Uses such as determining compounds that modulate the activity of NOV34 (p. 75), determining compounds that modulate the expression of NOV34 (p. 76), identifying binding partners of the encoded NOV34 polypeptide (p. 77), assaying for mutations in the NOV34 gene (p. 81), and using antibodies for the detection of NOV34 polypeptides (p. 82) are useful only in research to determine the function of the encoded protein itself. There is no "specific benefit in currently available form" to be derived from such studies. Tissue-specific expression such as that found on p. 705 is not specific to the claimed polynucleotide. It does not depend on any characteristics of the nucleic acid molecule itself. Further, while applicants list a number of diseases such as various neurological disorders, obesity, inflammatory diseases, and autoimmune

diseases for which the NOV34 gene may be useful in treatment (p. 705-706), the specification does not disclose any diseases or conditions known to be associated with the encoded protein. All Applicants have shown is varying expression of the claimed nucleic acid molecules in a number of cancer cell lines. Merely listing a number of possibilities is not sufficient to identify or confirm a "real world" context of use; clearly further research would be required to identify a disease in which the encoded protein is involved. Thus, significant further research is required to identify a disease for which it could be used, or a disease for which its presence would be diagnostic. See *Brenner v. Manson*, noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Further research would be required to determine how and if NOV34 is involved in the aforementioned diseases.

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. The specification fails to assert any activity for the encoded polypeptide other than those generally recognized to be attributes of connexin polypeptides. Identifying a nucleic acid molecule as encoding a polypeptide of this family does not endow the nucleic acid molecule with a specific and substantial utility. Connexins form multimeric assemblies known as connexons. Connexons form intercellular channels that permit the passage of ions, small metabolites and second messengers between the cytoplasms of adjacent cells. Bruzzone *et al.* (1997, *Eur. J. Neur.* 9: 1-6) teach that connexins form channels with different molecular size permeability, ionic selectivity, and gating properties, which indicates that the expression of one or another connexin type is not functionally equivalent (p. 1). Because of the differences in intercellular communication requirements, one connexin is not able to substitute for another (Curtin *et al.* (2002), *J. Cell Sci.* 115: 3379-3388). Thus, simply knowing that a polypeptide is homologous to a connexin does not impart a function on the polypeptide. Whether or not the connexin-like polypeptide formed homomeric or hetermeric connexons, it would not be known what ions or molecules are able to pass through the connexon. The biophysical and pharmacological characteristics of the connexin-like polypeptide could not be discerned by simply identifying it as a member of the connexin familiy. There is therefore no well-established utility for members of this family; utility is specific to the individual protein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-22 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Moreover, claims 13-15 and 17-22 are rejected under 35 U.S.C. 112, first paragraph because the specification, were it enabling for a nucleic acid molecule comprising SEQ ID NO: 111, would not reasonably provide enablement for fragments of SEQ ID NO: 111, nucleic acid molecules that are 85% identical to SEQ ID NO: 111, or nucleic acid molecules encoding polypeptides that are 85% or 90% identical to SEQ ID NO: 112 or variants of SEQ ID NO: 112. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The problem of predicting polypeptide structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the polypeptide is extremely complex. While it is known that many amino acid substitutions are generally possible in any given polypeptide, the positions within the polypeptide's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the polypeptide's structure/function relationship, such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions.

However, Applicants have provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the polypeptide that are tolerant to change and the nature and extent of changes that can be made in these positions. For instance, SEQ ID NO: 111 is 1253 nucleotides, and the polypeptide encoded by SEQ ID NO: 111 consists of 414 amino acids, a proposed connexin. Claims 13-15 and 17-22 are drawn to isolated nucleic acid molecules that are fragments of SEQ ID NO: 111, nucleic acid molecules that are 85% identical to SEQ ID NO: 111, or nucleic acid molecules encoding polypeptides that are 85% or 90% identical to SEQ ID NO: 112 or variants of SEQ ID NO: 112. There are no functional limitations in the claims. Moreover, the encoded polypeptides could have structures that are very different from that of SEQ ID NO: 112 with functions that are different from that of SEQ ID NO: 112. Regarding the claimed nucleic acid molecules comprising fragments of SEQ ID NO: 111, the specification provides no guidance as to which (if any) of the nucleotides can be changed or deleted to yield a functional equivalent of the polypeptide comprising SEQ ID NO: 112. More importantly, because there is no activity disclosed for the polypeptide comprising SEQ ID NO: 112, there would be no means for predicting or identifying other polypeptides that would have a similar activity. Even if an active site or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The claims are broad because they do not require the claimed polypeptide to be identical to the disclosed sequence and because the claims have no functional limitations.

Due to the large quantity of experimentation necessary to generate the infinite number of variants recited in the claims and screen the same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on polypeptide structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

In addition, claims 13-15 and 17-22 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to a genus, *i.e.* nucleic acid molecules encoding variants of SEQ ID NO: 112 (clone NOV34). The genus includes isolated nucleic acid molecules that are fragments of SEQ ID NO: 111, nucleic acid molecules that are 85% identical to SEQ ID NO: 111, and nucleic acid molecules encoding polypeptides that are 85% or 90% identical to SEQ ID NO: 112. Thus, the claims are drawn to a genus of nucleic acid molecules that is defined by sequence identity. Applicants have disclosed one species, the nucleic acid molecule consisting of SEQ ID NO: 111, but have not disclosed sufficient species for the broad genus which includes isolated nucleic acid molecules that are fragments of SEQ ID NO: 111, nucleic acid molecules that are 85% identical to SEQ ID NO: 111, and nucleic acid molecules encoding polypeptides that are 85% or 90% identical to SEQ ID NO: 112.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. The instant disclosure of a single species of nucleic acid molecule does not adequately describe the scope of the claimed genus, which encompasses hundreds of thousands of different nucleic acid molecules encoding polypeptides with varying structures and functions. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. Structural features that could distinguish the compounds in the genus from other nucleic acid molecules encoding connexin-like polypeptides are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teaching sufficient to enable one of skill to isolate and identify the nucleic acid molecules encompassed: there is no guidance in the art as to what the defining

characteristics of NOV34 might be. Thus, no identifying characteristics or properties of the instant nucleic acid molecules are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, the disclosure of SEQ ID NO: 111 is insufficient to describe the genus. Therefore, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acid molecules that comprise the nucleotide sequence of a naturally occurring allelic nucleic acid variant of SEQ ID NO: 111 or the nucleotide sequence encoding naturally occurring allelic variants of polypeptides comprising SEQ ID NO: 112. The factors to be considered when determining if there is adequate written description include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, Applicants provide no information as to the structures of the allelic variants. The only information provided is that they are allelic variants of NOV34. Applicants are claiming a species which has not been sufficiently described, i.e. Applicants are claiming sequences that have not yet been identified. Only once the nucleic acid molecules have been sequenced and their functions have been determine can a person of skill in the art determine that the nucleic acid molecules are allelic variants of NOV34. Accordingly, one of skill in the art would doubt that Applicants had possession of the claimed species at the time the application was filed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acid molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acid molecules comprising SEQ ID NO: 111 or encoding a polypeptide comprising SEQ ID NO: 112 but not the full breadth of the claim meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13 and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 is drawn to a "nucleic acid fragment encoding at least a portion of a polypeptide comprising the amino acid sequence given SEQ ID NO: 112, or any variant of said polypeptide wherein any amino acid of the chosen sequence is changed to a different amino acid, provided that no more than 10% of the amino acid residues in the sequence are so changed". It is not clear whether the fragment encodes a polypeptide that is at least 90% identical to SEQ ID NO: 112 or

whether the claim is drawn to a fragment of a nucleic acid molecule encoding a polypeptide at least 90% identical to SEQ ID NO: 112. Claim 17 is drawn to a "nucleic acid fragment wherein one or more nucleotides in the nucleotide sequence given SEQ ID NO: 111 is changed from that selected from the group consisting of the chosen sequence to a different nucleotide provided that no more than 15% of the nucleotides are so changed". Again, it is not clear whether the claim is drawn to a fragment of a nucleic acid molecule that is at least 85% identical to SEQ ID NO: 111 or whether the fragment itself is at least 85% identical to SEQ ID NO: 111. Similarly, claim 19 is drawn to a nucleic acid molecule wherein the "sequence is changed such that no more than 15% of the nucleotides in the coding sequence differ from the nucleotide sequence given SEQ ID NO: 111, or a fragment thereof". Again, it is not clear whether the claim is drawn to a fragment of a nucleotide sequence that is at least 85% identical to SEQ ID NO: 111 or whether the fragment itself is at least 85% identical to SEQ ID NO: 111.

Claim 18 is drawn to a nucleic acid molecule that hybridizes under stringent conditions to SEQ ID NO: 111 or a complement thereof. The term "stringent conditions" is a relative term which renders the claims indefinite. The term is not defined by the claim, and whereas the specification provides examples of stringent conditions (p. 29-30), the specification neither provides a definition of stringent conditions nor a standard for ascertaining the requisite degree, and one skilled in the art would not be reasonably apprised of the scope of the invention. It is unclear what amount hybridizing would occur under "stringent" conditions. One skilled in the art would not know what the metes and bounds of stringent conditions are.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Strausberg (GenBank Accession No. AI142991). Claims 17-22 are drawn to nucleic acid fragments of SEQ ID NO: 111, nucleic acid molecules that hybridize to SEQ ID NO: 111, fragments of nucleic acid

molecules that are at least 85% identical to SEQ ID NO: 111, vectors, and host cells. Strausberg teaches a complementary nucleic acid sequence that is 99.8% identical to SEQ ID NO: 111 from nucleotides 420-849 of SEQ ID NO: 111. The DNA was expressed in the vector pT7T3D. Thus, claims 17-22 are anticipated by Strausberg.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBK
2/19/04

JANET ANDRES
PATENT EXAMINER